DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
1401 Rockville Pike
Rockville MD 20852-1448

Reference Numbers: 97-1052 and 97-1065

Johan van Hoof, Ph.D.
SmithKline Beecham Biologicals
Rue de l'Institut 89
B-1330 Rixensart, Belgium

DEC 21 1998

Dear Dr. van Hoof:

Enclosed please find Biologics License Number 1090 issued in accordance with the provisions of Section 351(a) of the Public Health Service Act, as amended November 21, 1997 (Food and Drug Administration Modernization Act of 1997; Public Law 105-115), controlling the manufacture and sale of biological products. This license authorizes SmithKline Beecham Biologicals to manufacture and prepare Lyme Disease Vaccine (Recombinant OspA) for import into the United States, for sale, barter, or exchange.

Lyme Disease Vaccine (Recombinant OspA) is indicated for active immunization against Lyme disease in individuals 15-70 years of age. In accordance with your approved labeling, your product will bear the trade name LYMErix™ and will be marketed in single dose vials and pre-filled syringes.

The dating period for this product, in both single dose vials and pre-filled syringes, shall be 24 months from the date of manufacture when stored at 2-8° C. The date of manufacture is defined as the date of initiation of the earliest valid potency test. Any extension of the dating period will require the submission of supporting data as a supplement to your license application for review and approval. Alternatively, you may submit a stability protocol for prior approval to be used in extension of dating as a supplement to your license application.

You are required to submit to the Center for Biologics Evaluation and Research (CBER) samples of final container product for each future lot and the corresponding protocol showing the results of all applicable tests. No lots of product shall be distributed until notification of release is received from the Director, CBER.

We acknowledge your post-licensure commitments as indicated in the August 24, December 11, and December 17, 1998, submissions to your license application and which are as follows:

1. In order to obtain additional safety data, you have agreed to initiate a Phase 4 study, within 6 months post-licensure, as outlined in the December 11, 1998, submission to your license application. You are required to submit the final protocol to CBER for review and concurrence at least 30 days before planned initiation of the study; submit study reports annually to the product files; respond to CBER review comments; and amend the package insert as appropriate.

2. You have agreed to conduct reproductive toxicity testing within 6 months after licensure according to the protocol and contract with [redacted] submitted to your license application on December 11, 1998. Also, you have agreed to submit the results of this testing, and an appropriately revised package insert for approval when data from this testing are available.

3. You have agreed to establish and maintain a publicly known pregnancy registry to track the outcome of pregnancies in women vaccinated with Lyme Disease-Vaccine (Recombinant OspA). The existence of this registry will be noted in your approved package insert.

4. You have agreed to submit a completed study report concerning the cellular immunity study described in the document titled, "Report on Cellular Immunity to Outer-surface Protein A (OspA) in a Subset of Subjects in the SmithKline Beecham Lyme Disease Vaccine Trial #008," and submitted on June 23, 1998 (pp. 90-109) to your license application. The completed study report will be submitted to your product file within 6 months after licensure as agreed to in the August 24 and December 11, 1998, submissions to your license application.

5. You have agreed that at least two lots per year will be placed into your stability program. This is consistent with your stated commitment in your original submission and in the December 11, 1998, submission to your license application. If at any time a lot fails to meet the specifications in your stability protocol, you are requested to inform CBER immediately, and affected lots could be subject to recall.

Changes in the manufacturing, testing, packaging or labeling of your Lyme Disease Vaccine (Recombinant OspA), or in the manufacturing facilities, may require the submission of a supplement to your license application for our review and written approval prior to implementation.

It is requested that adverse experience reports for Lyme Disease Vaccine (recombinant OspA) be submitted in accordance with the adverse experience reporting requirements for licensed biological products (21 CFR 600.80) and that distribution reports be submitted as described (21 CFR 600.81). Since your product is categorized as a vaccine, these reports should be submitted to the Vaccine Adverse Event Reporting System (VAERS) using the pre-addressed form VAERS-1.

Please submit three copies of final printed labeling at the time of use and include part II of the label transmittal form with completed implementation information. In addition, please submit three copies of the introductory advertising and promotional labeling. You may wish to submit the proposed materials in draft form with an FDA Form 2567 to CBER, Advertising and Promotional Labeling Staff, HFM-202, 1401 Rockville Pike, Rockville, MD 20852-1448. Promotional claims should be consistent with and not contrary to approved labeling. No comparative claims or claim of superiority over other similar products should be made unless data to support such claims are submitted to and approved by CBER.

The supplement to your Establishment License Application to include areas for the manufacture of Lyme Disease Vaccine (Recombinant OspA) in your facility in Rixensart, Belgium, has been approved.

The information contained in the above referenced application and supplement will be included in your License file.

Please acknowledge receipt of this Biologics License to the Director, Division of Vaccines and Related Products Applications, HFM-475.

Sincerely yours,

Jerome A. Donlon, M.D., Ph.D.
Acting Director
Office of Compliance
and Biologics Quality
Center for Biologics
Evaluation and Research

M. Carolyn Hardegree, M.D
Director
Office of Vaccines
Research and Review
Center for Biologics
Evaluation and Research

cc: Dr. Paula Goldberg